



September 12, 2005

EUROPEAN PATENT OFFICE  
P.B. 5818  
Patentlaan 2  
GERMANY  
Fax: 31-70-340-3016  
Authorized Officer: Zervas, B.

Re: International Application No. PCT/IB2005/000872  
Warner-Lambert Company LLC  
Docket No. PC32134APCT

**RESPONSE TO WRITTEN OPINION OF THE INTERNATIONAL  
PRELIMINARY EXAMINING AUTHORITY**

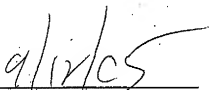
Dear Sirs,

This communication is being submitted in response to the Written Opinion of the International Searching Authority dated June 29, 2005. A Demand was filed for the above referenced application on June 15<sup>th</sup>, 2005. Thus, this communication is directed to the International Preliminary Examining Authority ("IPEA"). The IPEA has rejected claims 1, 3, 5, 6 and 8-9 as lacking novelty. The IPEA has acknowledged that claims 2, 4, 7, and 10-15 are novel and possess an inventive step.

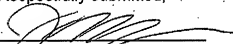
In order to advance the prosecution of this application, claim 1 has been amended. Claim 1, as amended, specifies that at least one of R<sup>1</sup> or R<sup>2</sup> must be represented by C<sub>1</sub>-C<sub>6</sub> alkyl, which may optionally be substituted. Support for this amendment may be found on page 13 of the specification, lines 5-7, where it

states that typically one of  $R^1$  or  $R^2$  will be  $C_1-C_6$  alkyl and the other may be hydrogen or  $C_1-C_6$  alkyl. The term "prodrug" has also been deleted from claim 1.

It is respectfully submitted that this amendment removes the novelty objections raised by the IPEA. The IPEA has acknowledged that claim 2, directed to a subgenus of lower alkyl's is novel and possess an inventive step. A positive International Preliminary Examiner Report is respectfully requested. Replacement pages 115 to 118 containing the amended claims accompany this letter.

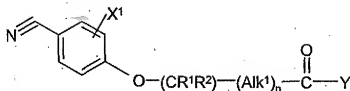
  
Date  
Warner-Lambert Company LLC  
Patent Department  
2800 Plymouth Road  
Ann Arbor, MI 48105  
(734) 622-1705

Respectfully submitted,

  
J. Michael Dixon  
Attorney for Applicant(s)  
Reg. No. 32,410

## CLAIMS

1. A compound of the formula:



in which;

- a)  $\text{X}^1$  is represented by cyano, halogen or haloalkyl,
- b) one of  $\text{R}^1$  or  $\text{R}^2$  is represented by  $\text{C}_1\text{-C}_6$  alkyl which may be optionally substituted, and the other of  $\text{R}^1$  or  $\text{R}^2$  is represented by hydrogen or  $\text{C}_1\text{-C}_6$  alkyl which may be optionally substituted,
- c)  $\text{Alk}^1$  is represented by a  $\text{C}_1\text{-C}_2$  linear alkylene group, in which up to two hydrogen atoms are optionally replaced by a substituent selected from the group consisting of  $\text{C}_1\text{-C}_6$  alkyl optionally substituted, halogen, hydroxy, thiol, and cyano,
- d)  $n$  is represented by the integer 0 or 1,
- e)  $\text{Y}$  is represented by  $\text{NX}^2\text{X}^3$  or  $\text{O-X}^3$ ,
- f)  $\text{X}^2$  is represented by hydrogen or  $(\text{C}_1\text{-C}_6)$  alkyl optionally substituted,
- g)  $\text{X}^3$  is represented by
- hydrogen,
  - $(\text{C}_1\text{-C}_{12})$  alkyl, optionally substituted,
  - $(\text{C}_2\text{-C}_{12})$  alkenyl, optionally substituted,
  - $(\text{C}_2\text{-C}_{12})$  alkynyl, optionally substituted,
  - $(\text{C}_3\text{-C}_{10})$  cycloalkyl, optionally substituted,
  - $(\text{C}_3\text{-C}_{10})$  cycloalkyl( $\text{C}_1\text{-C}_6$ ) alkyl, in which the alkyl and cycloalkyl moieties may each be optionally substituted,
  - $(\text{C}_6\text{-C}_{10})$  aryl, optionally substituted,

Print  
this

B

13

- viii.  $(C_6-C_{10})aryl(C_1-C_6)alkyl$ , in which the alkyl and aryl moieties may each be optionally substituted,
- ix.  $-(CH_2)_q-(Alk^2)-C(O)R^3$ , in which  $Alk^2$  is represented by a  $(C_1-C_6)$  linear alkylene group. In which up to eight hydrogen atoms may optionally be replaced by a substituent, selected from the group consisting of  $(C_1-C_6)$  alkyl optionally substituted,  $(C_1-C_6)$  alkoxy, halogen, hydroxy, thiol, cyano, and  $NR^8R^9$  in which  $R^8$  and  $R^9$  are each independently represented by hydrogen or  $(C_1-C_6)$  alkyl,  $q$  is the integer 0 or 1,  $R^3$  is represented by hydrogen,  $(C_1-C_{12})alkyl$ ,  $(C_6-C_{10})aryl$ , or  $(C_6-C_{10})aryl(C_1-C_6)alkyl$ , in which the alkyl and aryl moieties may each be optionally substituted,
- x.  $-(CH_2)_q-(Alk^2)-C(O)-O-R^4$ , in which  $Alk^2$  and  $q$  are as defined above, and  $R^4$  is represented by hydrogen,  $(C_1-C_{12})alkyl$ ,  $(C_6-C_{10})aryl$ , or  $(C_6-C_{10})aryl(C_1-C_6)alkyl$ , in which the alkyl and aryl moieties may be optionally substituted,
- xi.  $-(CH_2)_q-(Alk^2)-C(O)-NR^5R^6$  in which  $Alk^2$  and  $q$  are as described above, and  $R^5$  and  $R^6$  are each independently represented by hydrogen,  $(C_1-C_{12})alkyl$ ,  $(C_6-C_{10})aryl$ , or  $(C_6-C_{10})aryl(C_1-C_6)alkyl$ , in which the alkyl and aryl moieties may be optionally substituted,
- xii.  $-(CH_2)_q-(Alk^2)-Y-R^7$ , in which  $Alk^2$  and  $q$  are as defined above,  $Y$  is O or S, and  $R^7$  is selected from the group consisting of hydrogen,  $(C_1-C_{12})alkyl$ ,  $(C_6-C_{10})aryl$ , or  $(C_6-C_{10})aryl(C_1-C_6)alkyl$ , in which the alkyl and aryl moieties may be optionally substituted,
- xiii. heteroaryl, optionally substituted,
- xiv. heteroaryl $(C_1-C_6)alkyl$ , in which the heteroaryl and alkyl moieties may each be optionally substituted,

- xv. heterocyclic, optionally substituted,
- xvi. heterocyclic(C<sub>1</sub>-C<sub>6</sub>)alkyl, in which the alkyl  
and heterocyclic moieties may each be substituted, or,

- h) for those compounds in which Y is N, X<sup>2</sup> and X<sup>3</sup>, along with the adjacent nitrogen atom, may form a heterocyclic ring, which may optionally be substituted;  
or a salt or solvate thereof.
2. A compound according to claim 1 in which one of R<sup>1</sup> or R<sup>2</sup> is hydrogen and the other of R<sup>1</sup> or R<sup>2</sup> is selected from the group consisting of isobutyl, propyl, n-butyl, isopropyl, and ethyl.
  3. A compound according to claim 1 or 2 in which n is 0.
  4. A compound according to claim 1, 2, or 3 in which X<sup>1</sup> is trifluoromethyl and is located at the 3-position of the phenyl ring.
  5. A compound according to claim 1, 2, 3, or 4 in which Y is NX<sup>2</sup>X<sup>3</sup>.
  6. A compound according to claim 5 in which X<sup>2</sup> is hydrogen.
  7. A compound according to claim 6 in which X<sup>3</sup> is represented by a substituent selected from the group consisting of (C<sub>1</sub>-C<sub>12</sub>)alkyl, (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>6</sub>-C<sub>10</sub>)aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heteroaryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, and heterocyclic(C<sub>1</sub>-C<sub>6</sub>)alkyl.
  8. A compound according to claim 1, 2, 3, or 4 in which Y is OX<sup>3</sup>.
  9. A compound according to anyone of claims 1-8 in which X<sup>1</sup> is represented by halogen or haloalkyl.
  10. Use of a compound according to anyone of claims 1-9 as a medicine.

11. Use of a compound according to anyone of claims 1-9 in the manufacture of a medicament for inhibiting activation of the androgen receptor
12. Use of a compound according to anyone of claims 1-9 in the manufacture of a medicament for the alleviating a condition selected from the group consisting of hormone dependent cancers, benign hyperplasia of the prostate, acne, hirsutism, excess sebum, alopecia, premenstrual syndrome, lung cancer, precocious puberty, osteoporosis, hypogonadism, age-related decrease in muscle mass, and anemia.
13. A pharmaceutical composition comprising a compound according to anyone of claims 1-9 in admixture with 1, or more, pharmaceutically acceptable excipients.
14. A topical pharmaceutical formulation comprising a compound according to anyone of claims 1-9 in admixture with 1, or more, pharmaceutically acceptable excipients suitable for dermal application.
15. An article of manufacture comprising a compound according to anyone of claims 1-9 packaged for retail distribution, which advises a consumer how to utilize the compound to alleviate a condition selected from the group consisting of acne, alopecia, and oily skin.